Enthalpies of Transfer and the Solvent Dependency of the Conformational Enthalpy Term: the Cyclohexanol Equilibrium

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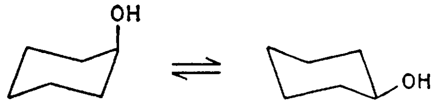
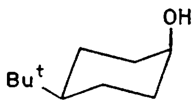
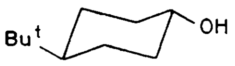
Summary Enthalpies of solution of *cis*- and *trans*-4-t-butylcyclohexanol provide quantitative evaluation of the effect of solvent on the ΔH° term for the conformational equilibrium of cyclohexanol.

We describe a novel approach for measuring solvent effects on the conformational enthalpy term. The method, which uses enthalpy of transfer data, offers significant advantages over the existing approach and is applicable, in principle, to any substituent. In this communication we illustrate its application to the cyclohexanol equilibrium (**1**) ⇌ (**2**).


(1) (2)


(3)


(4)

Let the enthalpy term (*i.e.*, the standard enthalpy change) for the equilibrium (**1**) ⇌ (**2**) in solvent *a* be denoted by ΔH°_a. The value of ΔH°_a will then be given by equation (1), where ΔH°_f terms are the standard enthalpy of formation of (**1**) and (**2**) in solvent *a*. Similarly for a second solvent *b*, equation (2) holds; subtracting equation (1) from (2) leads to equation (3). Now the term $\Delta H^\circ_b - \Delta H^\circ_a$ represents the solvent effect on ΔH°, which we shall refer to as $\delta\Delta H^\circ$, equation (4). The term $\Delta H^\circ_{fb} - \Delta H^\circ_{fa}$ for a given species is known as the enthalpy of transfer, ΔH°_t, of the species from solvent *a* to solvent *b*, equation (5). Introducing equation (4) and two equations of type (5) into (3) gives equation (6).

$$\Delta H^\circ_a = \Delta H^\circ_{fa}\,(\mathbf{2}) - \Delta H^\circ_{fa}\,(\mathbf{1}) \qquad (1)$$

$$\Delta H^\circ_b = \Delta H^\circ_{fb}\,(\mathbf{2}) - \Delta H^\circ_{fb}\,(\mathbf{1}) \qquad (2)$$

$$\Delta H^\circ_b - \Delta H^\circ_a = \Delta H^\circ_{fb}\,(\mathbf{2}) - \Delta H^\circ_{fa}\,(\mathbf{2}) - [\Delta H^\circ_{fb}\,(\mathbf{1}) - \Delta H^\circ_{fa}\,(\mathbf{1})] \qquad (3)$$

$$\Delta H^\circ_b - \Delta H^\circ_a = \delta\Delta H^\circ \qquad (4)$$

$$\Delta H^\circ_{fb} - \Delta H^\circ_{fa} = \Delta H^\circ_t \qquad (5)$$

$$\delta\Delta H^\circ = \Delta H^\circ_t\,(\mathbf{2}) - \Delta H^\circ_t\,(\mathbf{1}) \qquad (6)$$

In general, ΔH°_t values for a solute are experimentally obtainable from the difference in the enthalpies of solution, ΔH°_s, of the solute in the solvents concerned. However, in practice, the conformers (**1**) and (**2**) are physically inaccessible and instead we performed measurements on the fixed model compounds (**3**) and (**4**). This approach assumes that solvation about the t-butyl group in (**3**) and (**4**) does not interfere with solvation about the OH group or, if it does, then its contribution to ΔH°_t (**3**) and ΔH°_t (**4**) is the same, *i.e.* $\Delta H^\circ_t\,(\mathbf{4}) - \Delta H^\circ_t\,(\mathbf{3}) = \Delta H^\circ_t\,(\mathbf{2}) - \Delta H^\circ_t\,(\mathbf{1})$.

TABLE Enthalpies of solution and enthalpy of transfer data, in kcal mol^{-1}, for *cis*- and *trans*-4-t-butylcyclohexanol at 298·15 K[a]

Solvent	ΔH°_s(**3**)	ΔH°_s(**4**)	ΔH°_t(**3**)	ΔH°_t(**4**)	$\delta\Delta H^\circ$ [b]
n-Hexane	7·85	9·12	0	0	0
Ethyl acetate	5·80	6·00	−2·05	−3·12	−1·07
Acetone	5·88	5·96	−1·97	−3·16	−1·19
Benzene	7·36	7·34	−0·49	−1·78	−1·29
Chloroform	5·58	5·53	−2·27	−3·59	−1·32
Methanol	4·09	3·69	−3·76	−5·43	−1·67
Ethanol	3·81	3·11	−4·04	−6·01	−1·97

[a] Enthalpies of solution were determined using an LKB 8700 calorimetry system with an 8721-1 solution calorimeter. Thermochemical functions are expressed in terms of the defined calorie (4·1840 J) and refer to the isothermal process at 298·15 K. All measurements were corrected for the enthalpy of breaking of empty ampoules in the solvents concerned. The 95% confidence limits (Students t-test) of the ΔH°_s values average 0·05—0·06 kcal mol^{-1}, corresponding to 0·10—0·12 kcal mol^{-1} in the $\delta\Delta H^\circ$ values. [b] A negative value of $\delta\Delta H^\circ$ corresponds to stabilisation of (**4**) as compared with (**3**).

[At the least, the data provide an evaluation of the effect of solvent on ΔH° for the equilibrium between (**3**) and (**4**).] Enthalpies of solution for (**3**) and (**4**) and derived ΔH°_t data for transfer from n-hexane (the arbitrarily chosen standard solvent) to the remaining solvents are given in the Table. Values for the solvent effect term, $\delta\Delta H^\circ$, appear in the right hand column and show that $\delta\Delta H^\circ$ is the most negative (*i.e.*, the equatorial site is the most favoured) in ethanol. Discussion of trends however will be reserved for the full paper.

We believe the present method provides a convenient and valuable alternative to the classical approach involving measurements of K at different temperatures. Particular advantage lies in the use of low molarity solutions, *ca.* 0·008 M, which minimises solute–solute interactions. An earlier evaluation of $\delta\Delta H^\circ$ for the OH group involved direct equilibration (over Raney-nickel) of (**3**) and (**4**) as 0·05—0·20 M solutions.[1]

Work is now in progress to extend the treatment to other substituents as well as to other ring systems.†

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† For a comparable treatment of enthalpies of solution in a study of heteroaromatic tautomerism see M. J. Cook, A. R. Katritzky, L. G. Hepler, and T. Matsui, *Tetrahedron Letters*, 1976, 2685.

[1] E. L. Eliel and E. C. Gilbert, *J. Amer. Chem. Soc.*, 1969, **91**, 5487.